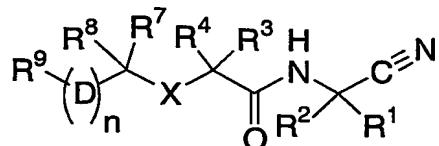


WHAT IS CLAIMED IS:

1. A compound of the formula:



5 wherein R¹ is hydrogen, C₁₋₆ alkyl or C₁₋₆ alkenyl wherein said alkyl and alkenyl groups are optionally substituted with halo;

R² is hydrogen, C₁₋₆ alkyl or C₁₋₆ alkenyl wherein said alkyl and alkenyl groups are optionally substituted with halo;

10 or R¹ and R² can be taken together with the carbon atom to which they are attached to form a C₃₋₈ cycloalkyl ring wherein said ring system is optionally substituted with C₁₋₆ alkyl, hydroxyalkyl or halo;

R³ is hydrogen, C₁₋₆ alkyl or C₁₋₆ alkenyl wherein said alkyl and alkenyl groups are optionally substituted with C₃₋₆ cycloalkyl or halo;

15 R⁴ is hydrogen, C₁₋₆ alkyl or C₁₋₆ alkenyl wherein said alkyl and alkenyl groups are optionally substituted with C₃₋₆ cycloalkyl or halo;

or R³ and R⁴ can be taken together with the carbon atom to which they are attached to form a C₃₋₈ cycloalkyl ring, C₅₋₈ cycloalkenyl ring, or five to seven membered heterocycloalkyl wherein said cycloalkyl, cycloalkenyl and heterocycloalkyl groups are optionally substituted with C₁₋₆ alkyl, halo, hydroxyalkyl, hydroxy, alkoxy or keto;

20 X is selected from the group consisting of -O-, -S-, SO₂, and -C(R⁵)(R⁶)-;

R⁵ is hydrogen or C₁₋₆ alkyl;

R⁶ is hydrogen or C₁₋₆ alkyl;

25 or R⁵ and R⁶ can be taken together with any of the atoms to which they may be attached or are between them to form a 3-8 membered cycloalkyl ring system wherein said ring system is optionally substituted with C₁₋₆ alkyl or halo;

R⁷ is hydrogen, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₁₋₆ alkyloxy, nitro, cyano, aryl, heteroaryl, C₃₋₈ cycloalkyl, heterocycloalkyl, -C(O)OR¹⁰, -C(O)R¹⁰, -C(O)OSi[CH(CH₃)₂]₃, -R¹⁰C(O)R¹³, -C(O)R¹³, -C(O)N(R¹²)(R¹²), -C(R¹⁰)(R¹¹)OH, -R¹⁰SR¹³, -R¹³, -C(R¹³)₃, -C(R¹⁰)(R¹¹)N(R¹³)₂, -C(R¹⁰)(R¹¹)N(R¹⁰)R¹³, -

C(R¹⁰)(R¹¹)N(R¹⁰)(R¹¹), -C(R¹⁰)(R¹¹)SC(R¹⁰)(R¹¹)(R¹³), -C(R^a)(R^b)NR^aC(R^a)(R^b), -C(R^a)(R^b)N(R^a)(R^b), -C(R^a)(R^b)C(R^a)(R^b)N(R^a)(R^b), -C(O)C(R^a)(R^b)N(R^a)(R^b), -C(R^a)(R^b)N(R^a)C(O) R¹³ or C(R^a)(R^b)C(O)N(R^a)(R^b); wherein said alkyl, alkenyl, alkynyl, haloalkyl, alkoxy, aryl, heteroaryl, cycloalkyl and heterocycloalkyl groups are optionally substituted on either the carbon or the heteroatom with one to five substituents independently selected from C₁₋₆ alkyl, halo, keto, cyano, haloalkyl, hydroxyalkyl, -OR⁹, -O(aryl), -NO₂, -NH₂, -NHS(O)₂R¹⁰, -R¹³SO₂R¹², -SO₂R¹², -SO(R¹²), -SO₂N(R^c)(R^d), -SO₂N(R¹⁰)C(O)(R¹²), -C(R¹⁰)(R¹¹)N(R¹⁰)(R¹¹), -C(R¹⁰)(R¹¹)OH, -COOH, -C(R^a)(R^b)C(O)N(R^a)(R^b), -N(R¹⁰)C(R¹⁰)(R¹¹)(R¹³), -NH(CH₂)₂OH, -NHC(O)OR¹⁰, -Si(CH₃)₃, heterocycloalkyl, aryl or heteroaryl;

R⁸ is hydrogen, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₁₋₆ alkyloxy, nitro, cyano, aryl, heteroaryl, C₃₋₈ cycloalkyl, heterocycloalkyl, -C(O)OR¹⁰, -C(O)R¹⁰, C(O)OSi[CH(CH₃)₂]₃, -R¹⁰C(O)R¹³, -C(O)R¹³, -C(O)N(R¹²)(R¹²), -C(R¹⁰)(R¹¹)OH, -R¹⁰SR¹³, -R¹³, -C(R¹³)₃, -C(R¹⁰)(R¹¹)N(R¹³)₂, -C(R¹⁰)(R¹¹)NR¹⁰C(R¹⁰)(R¹¹)R¹³, -C(R¹⁰)(R¹¹)N(R¹⁰)R¹³, -C(R¹⁰)(R¹¹)N(R¹⁰)(R¹¹), -C(R¹⁰)(R¹¹)SC(R¹⁰)(R¹¹)(R¹³), -C(R^a)(R^b)NR^aC(R^a)(R^b)(R¹³), -C(R^a)(R^b)N(R^a)(R^b), -C(R^a)(R^b)C(R^a)(R^b)N(R^a)(R^b), -C(O)C(R^a)(R^b)N(R^a)(R^b), -C(R^a)(R^b)N(R^a)C(O) R¹³ or C(R^a)(R^b)C(O)N(R^a)(R^b); wherein said alkyl, alkenyl, alkynyl, haloalkyl, alkoxy, aryl, heteroaryl, cycloalkyl and heterocycloalkyl groups are optionally substituted on either the carbon or the heteroatom with one to five substituents independently selected from C₁₋₆ alkyl, halo, keto, cyano, haloalkyl, hydroxyalkyl, -OR⁹, -O(aryl), -NO₂, -NH₂, -NHS(O)₂R¹⁰, -R¹³SO₂R¹², -SO₂R¹², SO(R¹²), -SO₂N(R^c)(R^d), -SO₂N(R¹⁰)C(O)(R¹²), -C(R¹⁰)(R¹¹)N(R¹⁰)(R¹¹), -C(R¹⁰)(R¹¹)OH, -COOH, -C(R^a)(R^b)C(O)N(R^a)(R^b), -N(R¹⁰)C(R¹⁰)(R¹¹)(R¹³), -NH(CH₂)₂OH, -NHC(O)OR¹⁰, -Si(CH₃)₃, heterocycloalkyl, aryl or heteroaryl;

D is aryl, heteroaryl, C₃₋₈ cycloalkyl, heterocycloalkyl, C₁₋₃ alkyl or C₁₋₃ alkenyl wherein said aryl, heteroaryl, cycloalkyl and heterocycloalkyl groups, which may be monocyclic or bicyclic, are optionally substituted on either the carbon or the heteroatom with one to three substituents selected from C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkyloxy, halo, keto, nitro, cyano, aryl, heteroaryl, C₃₋₈ cycloalkyl, heterocyclyl, -C(O)OR¹⁰, -C(O)OSi[CH(CH₃)₂]₃, -OR¹⁰, -C(O)R¹⁰, -R¹⁰C(O)R¹³, -C(O)R¹³, -C(O)N(R¹²)(R¹²), -C(R¹⁰)(R¹¹)OH, -SR¹², -SR¹³, -R¹⁰SR¹³, -R¹³, -C(R¹³)₃, -C(R¹⁰)(R¹¹)N(R¹³)₂, -SO₂R¹², -SO(R¹²), -SO₂R¹³, -SO₂N(R^c)(R^d), -SO₂CH(R¹⁰)(R¹¹), -SO₂N(R¹⁰)C(O)(R¹²), -SO₂(R¹⁰)C(O)N(R¹²)₂, -OSO₂R¹⁰, -N(R¹⁰)(R¹¹), -N(R¹⁰)C(O)NR¹⁰R¹³, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)OR¹⁰,

N(R¹⁰)SO₂R¹⁰, -C(R¹⁰)(R¹¹)NR¹⁰C(R¹⁰)(R¹¹)R¹³, -C(R¹⁰)(R¹¹)N(R¹⁰)R¹³, -C(R¹⁰)(R¹¹)N(R¹⁰)(R¹¹), -C(R¹⁰)(R¹¹)SC(R¹⁰)(R¹¹)(R¹³), R¹⁰S-, -C(R^a)(R^b)NR^aC(R^a)(R^b)(R¹³), -C(R^a)(R^b)N(R^a)(R^b), -C(R^a)(R^b)C(R^a)(R^b)N(R^a)(R^b), -C(O)C(R^a)(R^b)N(R^a)(R^b), -C(R^a)(R^b)N(R^a)C(O)R¹³ or -C(R^a)(R^b)C(O)N(R^a)(R^b); wherein

- 5 said alkyl, alkenyl, alkynyl, haloalkyl, alkoxy, aryl, heteroaryl, cycloalkyl and heterocyclyl groups are optionally substituted on either the carbon or the heteroatom with one to five substituents independently selected from C₁-₆ alkyl, C₃-₈ cycloalkyl, halo, keto, cyano, haloalkyl, hydroxyalkyl, -OR¹³, -NO₂, -NH₂, -NHS(O)₂R¹⁰, -R¹³SO₂R¹², -SO₂R¹², -SO(R¹²), -SO₂N(R^c)(R^d), -SO₂N(R¹⁰)C(O)(R¹²), -C(R¹⁰)(R¹¹)N(R¹⁰)(R¹¹), -C(R¹⁰)(R¹¹)OH, -COOH, -C(R^a)(R^b)C(O)N(R^a)(R^b), -N(R¹⁰)C(R¹⁰)(R¹¹), -NH(CH₂)₂OH, -NHC(O)OR¹⁰, -Si(CH₃)₃, heterocycloalkyl, aryl or heteroaryl;

R⁹ is hydrogen, hydroxy, cyano, C₁-₆ alkyl, C₂-₆ alkenyl, C₂-₆ alkynyl, C₁-₆ alkyloxy, halo, aryl, heteroaryl, C₃-₈ cycloalkyl, heterocycloalkyl, -C(O)OR¹⁰, -OR¹⁰, -C(O)R¹⁰, -C(O)R¹³, -

- 15 C(O)N(R¹²)(R¹²), -C(R¹⁰)(R¹¹)OH, -R¹⁰SR¹³, -R¹³, -C(R¹³)₃, -C(R¹⁰)(R¹¹)N(R¹³)₂, SR¹⁰, -SO₂R¹², -SO(R¹²), -SO₂R¹³, -SO₂N(R^c)(R^d), -SO₂CH(R¹⁰)(R¹¹), -N(R¹⁰)(R¹¹), -N(R¹⁰)C(O)NR¹⁰R¹³, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)OR¹⁰, -N(R¹⁰)SO₂R¹⁰, -

C(R¹⁰)(R¹¹)NR¹⁰C(R¹⁰)(R¹¹)R¹³, -C(R¹⁰)(R¹¹)N(R¹⁰)R¹³, -C(R¹⁰)(R¹¹)N(R¹⁰)(R¹¹), -C(R¹⁰)(R¹¹)SC(R¹⁰)(R¹¹)-, R¹⁰S-, -C(R^a)(R^b)NR^aC(R^a)(R^b), -C(R^a)(R^b)N(R^a)(R^b), -

- 20 C(R^a)(R^b)C(R^a)(R^b)N(R^a)(R^b), -C(O)C(R^a)(R^b)N(R^a)(R^b), -C(R^a)(R^b)N(R^a)C(O)R¹³; wherein said alkyl, alkenyl, alkynyl, alkoxy, aryl, heteroaryl, cycloalkyl and heterocycloalkyl groups are optionally substituted on either the carbon or the heteroatom with one to five substituents independently selected from C₁-₆ alkyl, C₃-₈ cycloalkyl, halo, keto, cyano, haloalkyl, hydroxyalkyl, -OR¹³, -NO₂, -NH₂, -NHS(O)₂R⁸, -R¹³SO₂R¹², SO₂R¹², SO(R¹²), -
- 25 SO₂N(R^c)(R^d), SO₂N(R¹⁰)C(O)(R¹²), -C(R¹⁰)(R¹¹)N(R¹⁰)(R¹¹), -C(R¹⁰)(R¹¹)OH, -COOH, -C(R^a)(R^b)C(O)N(R^a)(R^b), -N(R¹⁰)C(R¹⁰)(R¹¹), -NH(CH₂)₂OH, -NHC(O)OR¹⁰, Si(CH₃)₃, heterocycloalkyl, aryl or heteroaryl;

R¹⁰ is hydrogen or C₁-₆ alkyl;

- 30 R¹¹ is hydrogen or C₁-₆ alkyl;

R¹² is hydrogen or C₁-₆ alkyl which is optionally substituted with halo, alkoxy, cyano, -NR¹⁰ or -SR¹⁰;

R₁₃ is selected from the group consisting of hydrogen, aryl, aryl(C₁₋₄) alkyl, heteroaryl, heteroaryl(C₁₋₄)alkyl, C₃₋₈cycloalkyl, C₃₋₈cycloalkyl(C₁₋₄)alkyl, and heterocycloalkyl(C₁₋₄)alkyl wherein said groups can be optionally substituted with halo or alkoxy;

5 Ra is hydrogen, C₁₋₆ alkyl, (C₁₋₆ alkyl)aryl, (C₁₋₆ alkyl)hydroxyl, -O(C₁₋₆ alkyl), hydroxyl, halo, aryl, heteroaryl, C₃₋₈ cycloalkyl, heterocycloalkyl, wherein said alkyl, aryl, heteroaryl, C₃₋₈ cycloalkyl and heterocycloalkyl can be optionally substituted on either the carbon or the heteroatom with C₁₋₆ alkyl or halo;

10 Rb is hydrogen, C₁₋₆ alkyl, (C₁₋₆ alkyl)aryl, (C₁₋₆ alkyl)hydroxyl, alkoxy, hydroxyl, halo, aryl, heteroaryl, C₃₋₈ cycloalkyl, heterocycloalkyl, wherein said alkyl, aryl, heteroaryl, C₃₋₈ cycloalkyl and heterocycloalkyl can be optionally substituted on either the carbon or the heteroatom with C₁₋₆ alkyl or halo;

15 or R^a and R^b can be taken together with the carbon atom to which they are attached or are between them to form a C₃₋₈ cycloalkyl ring or C₃₋₈ heterocycloalkyl ring wherein said 3-8 membered ring system may be optionally substituted with C₁₋₆ alkyl and halo;

Rc is hydrogen or C₁₋₆ alkyl which is optionally substituted with halo or OR₁₃;

Rd is hydrogen or C₁₋₆ alkyl which is optionally substituted with halo or OR₁₃;

20 or Rc and Rd can be taken together with the nitrogen atom to which they are attached or are between them to form a C₃₋₈ heterocycloalkyl ring which is optionally substituted with C₁₋₆ alkyl, halo hydroxyalkyl, hydroxy, alkoxy or keto;

n is zero, one, two or three;

25 and the pharmaceutically acceptable salts, stereoisomers and N-oxide derivatives thereof.

2. The compound of Claim 1 wherein R³ is H and R⁴ is C₁₋₆ alkyl which is optionally substituted with C₃₋₆ cycloalkyl or halo; and the pharmaceutically acceptable salts, stereoisomers and N-oxide derivatives thereof.

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3. The compound of Claim 2 wherein R³ is H and R⁴ is isobutyl; and the pharmaceutically acceptable salts, stereoisomers and N-oxide derivatives thereof.

35 4. The compound of Claim 1 wherein R¹ and R² are each H; and the pharmaceutically acceptable salts, stereoisomers and N-oxide derivatives thereof.

5. The compound of Claim 1 wherein R¹ and R² can be taken together with the carbon atom to which they are attached to form a C₃-8 cycloalkyl ring wherein said ring system is optionally substituted with C₁-6 alkyl, hydroxyalkyl or halo; and the pharmaceutically acceptable salts, stereoisomers and N-oxide derivatives thereof.

6. The compound of Claim 5 wherein R¹ and R² can be taken together with the carbon atom to which they are attached to form a cyclopropyl ring wherein said ring system is optionally substituted with C₁-6 alkyl or halo; and the pharmaceutically acceptable salts, stereoisomers and N-oxide derivatives thereof.

7. The compound of Claim 1 wherein X is O; and the pharmaceutically acceptable salts, stereoisomers and N-oxide derivatives thereof.

15 8. The compound of Claim 7 wherein R⁷ is aryl, heteroaryl or C₁-6 haloalkyl and R⁸ is hydrogen; and the pharmaceutically acceptable salts, stereoisomers and N-oxide derivatives thereof.

20 9. The compound of Claim 1 wherein D is aryl, heteroaryl, cycloalkyl or heterocycloalkyl; and the pharmaceutically acceptable salts, stereoisomers and N-oxide derivatives thereof.

25 10. The compound of Claim 9 wherein D is phenyl or pyridyl; and the pharmaceutically acceptable salts, stereoisomers and N-oxide derivatives thereof.

11. The compound of Claim 1 wherein R⁹ is aryl, heteroaryl or heterocycloalkyl, wherein wherein said groups are optionally substituted on either the carbon or the heteroatom with one to five substituents independently selected from C₁-6 alkyl, halo, -SO₂R¹², -SO(R¹²) or aryl; and the pharmaceutically acceptable salts, stereoisomers and N-oxide derivatives thereof.

12. The compound of Claim 1 selected from:
(2S)-2-{[(R)-(4-bromophenyl)(phenyl)methyl]oxy}-N-(cyanomethyl)-4-methylpentanamide;

(2S)-N-(cyanomethyl)-4-methyl-2-{[(R)-phenyl(4'-piperazin-1-yl-1,1'-biphenyl-4-yl)methyl]oxy}pentanamide;

5 (2S)-N-(cyanomethyl)-4-methyl-2-{[(R)-phenyl(4'-pyridin-4-yl-1,1'-biphenyl-4-yl)methyl]oxy}pentanamide;

(2S)-2-{[(R)-(4-bromophenyl)[4-(methylsulfonyl)phenyl]methyl]oxy}-N-(cyanomethyl)-4-methylpentanamide;

10 (2S)-N-(cyanomethyl)-4-methyl-2-{[(S)-[4-(methylsulfonyl)phenyl](4'-piperazin-1-yl-1,1'-biphenyl-4-yl)methyl]oxy}pentanamide;

(2S)-N-(cyanomethyl)-2-{[(R)-[4'-(1H-imidazol-1-yl)-1,1'-biphenyl-4-yl](phenyl)methyl]oxy}-4-methylpentanamide;

15 (2S)-2-{[(R)-(4-bromophenyl)(4-chlorophenyl)methyl]oxy}-N-(cyanomethyl)-4-methylpentanamide;

(2S)-2-{[(S)-(4-bromophenyl)(mesityl)methyl]oxy}-N-(cyanomethyl)-4-methylpentanamide;

20 (2S)-2-(benzhydryloxy)-N-(cyanomethyl)-4-methylpentanamide;

(2S)-2-{[(S)-(4-chlorophenyl)(4'-piperazin-1-yl-1,1'-biphenyl-4-yl)methyl]oxy}-N-(cyanomethyl)-4-methylpentanamide;

25 (2S)-N-(cyanomethyl)-2-{[(S)-mesityl(4'-piperazin-1-yl-1,1'-biphenyl-4-yl)methyl]oxy}-4-methylpentanamide;

1-{[(R)-(4-bromophenyl)(phenyl)methyl]oxy}-N-(cyanomethyl)cyclohexanecarboxamide;

30 (2S)-2-{[(1R)-1-(4-bromophenyl)-2-(4-chlorophenyl)ethyl]oxy}-N-(cyanomethyl)-4-methylpentanamide;

(2S)-2-{[(R)-(4-bromophenyl)(cyclopropyl)methyl]oxy}-N-(cyanomethyl)-4-methylpentanamide;

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(2S)-2-{[(R)-(3-bromophenyl)(phenyl)methyl]oxy}-N-(cyanomethyl)-4-methylpentanamide;

2-[(4-bromophenyl)(1-methyl-1H-pyrazol-5-yl)methoxy]-N-(cyanomethyl)-4-
5 methylpentanamide;

2-[(4-bromophenyl)(1-methyl-1H-pyrazol-5-yl)methoxy]-N-(cyanomethyl)-4-
methylpentanamide;

10 (2S)-2-[[4-(3-chloropyrazin-2-yl)phenyl](phenyl)methoxy]-N-(cyanomethyl)-4-
methylpentanamide;

(2S)-N-(cyanomethyl)-4-methyl-2-{phenyl[4-(1,3-thiazol-2-yl)phenyl]methoxy}pentanamide;

15 (2S)-2-[[4'-(aminosulfonyl)-1,1'-biphenyl-4-yl](phenyl)methoxy]-N-(cyanomethyl)-4-
methylpentanamide;

(2S)-N-(cyanomethyl)-4-methyl-2-[[4'-(methylsulfonyl)-1,1'-biphenyl-4-
yl](phenyl)methoxy]pentanamide;

20 (2S)-N-(cyanomethyl)-4-methyl-2-[phenyl(4-quinolin-3-ylphenyl)methoxy]pentanamide;

(2S)-N-(cyanomethyl)-4-methyl-2-[phenyl(4-pyrimidin-5-ylphenyl)methoxy]pentanamide;

25 (2S)-N-(cyanomethyl)-4-methyl-2-[phenyl(4-quinolin-8-ylphenyl)methoxy]pentanamide;

(2S)-N-(cyanomethyl)-2-[(4-[6-(hydroxymethyl)-1-oxidopyridin-3-yl]phenyl)(phenyl)methoxy]-
4-methylpentanamide;

30 (2S)-N-(cyanomethyl)-4-methyl-2-[phenyl(4-pyridin-4-ylphenyl)methoxy]pentanamide;

(2S)-N-(cyanomethyl)-2-[[4-(1H-indol-4-yl)phenyl](phenyl)methoxy]-4-methylpentanamide;

(2S)-N-(cyanomethyl)-4-methyl-2-[phenyl(4-pyridin-2-ylphenyl)methoxy]pentanamide;

(2S)-N-(cyanomethyl)-4-methyl-2-[phenyl(4-pyrazin-2-ylphenyl)methoxy]pentanamide;

(2S)-N-(cyanomethyl)-4-methyl-2-[phenyl(4-pyridin-3-ylphenyl)methoxy]pentanamide;

5 (2S)-N-(cyanomethyl)-4-methyl-2-(phenyl{4-[5-(2H-tetraazol-5-yl)pyridin-3-yl]phenyl}methoxy)pentanamide;

(2S)-N-(cyanomethyl)-4-methyl-2-[[4-(3-methylpyridin-2-yl)phenyl](phenyl)methoxy]pentanamide;

10 2-{4-[[((1S)-1-{{(cyanomethyl)amino}carbonyl}-3-methylbutyl)oxy](phenyl)methyl]phenyl}isonicotinic acid;

(2S)-N-(cyanomethyl)-4-methyl-2-[phenyl(4-pyrimidin-2-ylphenyl)methoxy]pentanamide;

15 ethyl 4'-{{((1S)-1-{{(cyanomethyl)amino}carbonyl}-3-methylbutyl)oxy}(phenyl)methyl}-1,1'-biphenyl-4-carboxylate;

20 4'-{{((1S)-1-{{(cyanomethyl)amino}carbonyl}-3-methylbutyl)oxy}(phenyl)methyl}-1,1'-biphenyl-4-carboxamide;

N-(cyanomethyl)-4-methyl-2-{phenyl[4-(piperazin-1-ylcarbonyl)phenyl]methoxy}pentanamide;

25 N-(cyanomethyl)-2-[(4-{{[4-(2-fluoroethyl)piperazin-1-yl]carbonyl}phenyl}(phenyl)methoxy]-4-methylpentanamide;

N-(cyanomethyl)-4-methyl-2-[(4-{{[4-(methylsulfonyl)piperazin-1-yl]carbonyl}phenyl}(phenyl)methoxy]pentanamide;

30 (2S)-2-{{(S)-(4-bromophenyl)(thien-2-yl)methyl}oxy}-N-(cyanomethyl)-4-methylpentanamide;

(2S)-N-(cyanomethyl)-4-methyl-2-{{(S)-(4'-piperazin-1-yl-1,1'-biphenyl-4-yl)(thien-2-yl)methyl}oxy}pentanamide;

35 (2S)-2-[(4-bromophenyl)(thien-3-yl)methoxy]-N-(cyanomethyl)-4-methylpentanamide;

2-[(4-bromophenyl)(pyridin-2-yl)methoxy]-N-(cyanomethyl)-4-methylpentanamide;

2-[(4-bromophenyl)(1,3-thiazol-2-yl)methoxy]-N-(cyanomethyl)-4-methylpentanamide;

5 N-(cyanomethyl)-4-methyl-2-[(4'-piperazin-1-yl-1,1'-biphenyl-4-yl)(pyridin-2-yl)methoxy]pentanamide;

10 N-(cyanomethyl)-4-methyl-2-[(4'-piperazin-1-yl-1,1'-biphenyl-4-yl)(1,3-thiazol-2-yl)methoxy]pentanamide;

2-[(4-bromophenyl)(pyridin-3-yl)methoxy]-N-(cyanomethyl)-4-methylpentanamide;

2-[(4-bromophenyl)(pyridin-4-yl)methoxy]-N-(cyanomethyl)-4-methylpentanamide;

15 2-[1-(4-bromophenyl)ethoxy]-N-(cyanomethyl)-4-methylpentanamide;

2-[1-(4-bromophenyl)propoxy]-N-(cyanomethyl)-4-methylpentanamide;

20 2-[1-(4-bromophenyl)ethoxy]-N-(cyanomethyl)-4-methylpentanamide;

N-(cyanomethyl)-2-[(4-fluorophenyl)(4-pyridin-4-ylphenyl)methoxy]-4-methylpentanamide;

2-[(4-bromophenyl)(4-fluorophenyl)methoxy]-N-(cyanomethyl)-4-methylpentanamide;

25 2-[(4-bromophenyl)(4-fluorophenyl)methoxy]-N-(1-cyanocyclopropyl)-4-methylpentanamide;

N-(cyanomethyl)-2-[(4-fluorophenyl)(4'-piperazin-1-yl-1,1'-biphenyl-4-yl)methoxy]-4-methylpentanamide;

30 2-[1-(4-bromophenyl)propoxy]-N-(cyanomethyl)-4-methylpentanamide;

N-(1-cyanocyclopropyl)-2-[(4-fluorophenyl)(4'-piperazin-1-yl-1,1'-biphenyl-4-yl)methoxy]-4-methylpentanamide;

35

N-(cyanomethyl)-4-methyl-2-[phenyl(4'-piperazin-1-yl-1,1'-biphenyl-4-yl)methoxy]pentanamide;

(2S)-N-(cyanomethyl)-2-[(4-fluorophenyl)(4'-piperazin-1-yl-1,1'-biphenyl-4-yl)methoxy]-4-methylpentanamide;

5

(2S)-N-(cyanomethyl)-4-methyl-2-[phenyl(4'-piperazin-1-yl-1,1'-biphenyl-4-yl)methoxy]pentanamide;

(2S)-2-[(4-bromophenyl)(phenyl)methoxy]-N-(cyanomethyl)-4-methylpentanamide;

10

(2S)-N-(cyanomethyl)-4-methyl-2-{{(S)-phenyl(4'-piperazin-1-yl-1,1'-biphenyl-4-yl)methyl}oxy}pentanamide;

N-(cyanomethyl)-4-methyl-2-[1-(4'-piperazin-1-yl-1,1'-biphenyl-4-yl)ethoxy]pentanamide;

15

N-(cyanomethyl)-4-methyl-2-[1-(4'-piperazin-1-yl-1,1'-biphenyl-4-yl)ethoxy]pentanamide;

(2S)-2-[(4-bromophenyl)(4-fluorophenyl)methoxy]-N-(cyanomethyl)-4-methylpentanamide;

20

(2S)-N-(Cyanomethyl)-4-methyl-2-{{(R)-[4'-(methylthio)-1,1'-biphenyl-4-yl](phenyl)methyl}oxy}pentanamide;

(2S)-N-(cyanomethyl)-4-methyl-2-{{(R)-[4'-(methylsulfonyl)-1,1'-biphenyl-4-yl](phenyl)methyl}oxy}pentanamide;

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(2S)-N-(Cyanomethyl)-4-methyl-2-{{(R)-(4'-morpholin-4-yl-1,1'-biphenyl-4-yl)(phenyl)methyl}oxy}pentanamide;

(2S)-2-[(4-bromophenyl)(cyclohexyl)methoxy]-N-(cyanomethyl)-4-methylpentanamide;

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(2S)-2-[(4-bromophenyl)(cyclohexyl)methoxy]-N-(cyanomethyl)-4-methylpentanamide;

(2S)-2-{{1-(4-bromophenyl)-2-methylprop-2-enyl}oxy}-N-(cyanomethyl)-4-methylpentanamide;

35 (2S)-2-{{1-(4-bromophenyl)-2-methylprop-2-enyl}oxy}-N-(cyanomethyl)-4-methylpentanamide;

(2S)-2-[1-(4-bromophenyl)-2-methylpropoxy]-N-(cyanomethyl)-4-methylpentanamide;

(2S)-2-[1-(4-bromophenyl)-2-methylpropoxy]-N-(cyanomethyl)-4-methylpentanamide;

5 2-[1-(4-bromophenyl)-2,2,2-trifluoroethoxy]-N-(cyanomethyl)-4-methylpentanamide;

(2S)-N-(cyanomethyl)-2-{[(R)-(4-cyanophenyl)(phenyl)methyl]oxy}-4-methylpentanamide;

10 (2S)-N-(cyanomethyl)-4-methyl-2-[((R)-phenyl{4-[(trimethylsilyl)ethynyl]phenyl}methyl)oxy]pentanamide;

(2S)-N-(cyanomethyl)-2-{[(R)-(4-ethynylphenyl)(phenyl)methyl]oxy}-4-methylpentanamide;

15 2-[1-(4-bromophenyl)-2,2,2-trifluoroethoxy]-N-(cyanomethyl)-4-methylpentanamide;

N-(cyanomethyl)-4-methyl-2-[2,2,2-trifluoro-1-(4'-piperazin-1-yl-1,1'-biphenyl-4-yl)ethoxy]pentanamide;

20 2-{[(S)-(4-bromophenyl)(phenyl)methyl]oxy}-N-(cyanomethyl)-4-methylpentanamide;

2-[1-(4-bromophenyl)(phenyl)methoxy]-N-(cyanomethyl)-4-methylpentanamide;

N-(cyanomethyl)-4-methyl-2-[phenyl(4-pyridin-4-ylphenyl)methoxy]pentanamide;

25 N-(cyanomethyl)-4-methyl-2-[phenyl(4'-piperazin-1-yl-1,1'-biphenyl-4-yl)methoxy]pentanamide;

(2R)-2-[(4-bromophenyl)(4-fluorophenyl)methoxy]-N-(cyanomethyl)-4-methylpentanamide;

30 (2S)-N-(cyanomethyl)-4-methyl-2-{[(R)-{4'-[4-(methylsulfonyl)piperazin-1-yl]-1,1'-biphenyl-4-yl}(phenyl)methyl]oxy}pentanamide;

2-{[(4-bromophenyl)(phenyl)methyl]thio}-N-(cyanomethyl)-4-methylpentanamide;

(2S)-N-(cyanomethyl)-4-methyl-2-{[(R)-[4'-(4-methylpiperazin-1-yl)-1,1'-biphenyl-4-yl](phenyl)methyl]oxy}pentanamide;

5 N-(cyanomethyl)-4-methyl-2-(2,2,2-trifluoro-1-{4'-[4-(methylsulfonyl)piperazin-1-yl]-1,1'-biphenyl-4-yl}ethoxy)pentanamide;

2-[(4-bromophenyl)(2,4,6-trifluorophenyl)methoxy]-N-(cyanomethyl)-4-methylpentanamide;

10 (2S)-2-[bis(4-bromophenyl)methoxy]-N-(cyanomethyl)-4-methylpentanamide;

10 (2S)-N-(cyanomethyl)-4-methyl-2-{[(R)-phenyl(4-pyridin-4-ylphenyl)methyl]oxy}pentanamide;
4-{4'-[{(R)-[((1S)-1-[(cyanomethyl)amino]carbonyl)-3-methylbutyl]oxy}(phenyl)methyl]-1,1'-biphenyl-4-yl}-1,1-dimethylpiperazin-1-ium iodide;

15 (2S)-N-(cyanomethyl)-2-{[(R)-{4'-[4-(2-hydroxyethyl)piperazin-1-yl]-1,1'-biphenyl-4-yl}(phenyl)methyl]oxy}-4-methylpentanamide;

20 2-[(4-bromophenyl)(phenyl)methylsulfonyl]-N-(cyanomethyl)-4-methylpentanamide;

20 N-(cyanomethyl)-4-methyl-2-{2,2,2-trifluoro-1-[4'-(methylthio)-1,1'-biphenyl-4-yl]ethoxy}pentanamide;

25 2-[1-(4-bromophenyl)-2,2,2-trifluoroethoxy]-N-(1-cyanocyclopropyl)-4-methylpentanamide;

25 N-(cyanomethyl)-4-methyl-2-{2,2,2-trifluoro-1-[4'-(methylsulfonyl)-1,1'-biphenyl-4-yl]ethoxy}pentanamide;

30 4-[((1S)-1-[(cyanomethyl)amino]carbonyl)-3-methylbutyl] oxy(phenyl)methyl]-N-methoxy-N-methylbenzamide;

4-[((1S)-1-[(cyanomethyl)amino]carbonyl)-3-methylbutyl]oxy] (phenyl)methyl]-N,N-dimethylbenzamide;

(2S)-N-(cyanomethyl)-4-methyl-2-[[4-(morpholin-4-ylcarbonyl)phenyl](phenyl)methoxy]pentanamide;

4-[[((1S)-1-[(cyanomethyl)amino]carbonyl)-3-methylbutyl]oxy] (phenyl)methyl]benzoic acid;

(2S)-N-(cyanomethyl)-4-methyl-2-{{(R)-{4-[4-(methylthio)benzoyl]phenyl}(phenyl)methyl}oxy}pentanamide;

(2S)-N-(cyanomethyl)-4-methyl-2-{{(R)-{4-[4-(methylsulfonyl)benzoyl]phenyl}(phenyl)methyl}oxy}pentanamide;

(2S)-2-{{(R)-[4-(1,1'-biphenyl-4-ylcarbonyl)phenyl](phenyl)methyl}oxy}-N-(cyanomethyl)-4-methylpentanamide;

(2S)-2-[(5-bromopyridin-2-yl)(phenyl)methoxy]-N-(cyanomethyl)-4-methylpentanamide;

(2S)-N-(cyanomethyl)-4-methyl-2-{{phenyl}[5-(4-piperazin-1-ylphenyl)pyridin-2-yl]methoxy}pentanamide;

(2S)-N-(cyanomethyl)-4-methyl-2-{{5-[4-(methylthio)phenyl]pyridin-2-yl}(phenyl)methoxy}pentanamide;

(2S)-N-(cyanomethyl)-4-methyl-2-{{5-[4-(methylsulfonyl)phenyl]pyridin-2-yl}(phenyl)methoxy}pentanamide;

(2S)-N-(cyanomethyl)-4-methyl-2-{{[R or S]-{5-[4-(methylsulfonyl)phenyl]pyridin-2-yl}(phenyl)methyl}oxy}pentanamide;

(2S)-N-(cyanomethyl)-4-methyl-2-{{[(R or S)-{5-[4-methylsulfonyl]phenyl}pyridin-2-yl](phenyl)methyl}oxy}pentanamide;

(2S)-N-(cyanomethyl)-4-methyl-2-{{5-[4-(methylsulfonyl)phenyl]1-oxidopyridin-2-yl}(phenyl)methoxy}pentanamide;

(2S)-2-[(4-bromothien-2-yl)(phenyl)methoxy]-N-(cyanomethyl)-4-methyl pentanamide;

(2S)-2-[(5-bromo-1-oxidopyridin-2-yl)(phenyl)methoxy]-N-(cyanomethyl)-4-methylpentanamide;

5 (2S)-N-(cyanomethyl)-4-methyl-2-{[(R)-[4-(1-methylpiperidin-4-yl)phenyl](phenyl)methyl]oxy}pentanamide;

(2S)-N-(cyanomethyl)-2-{[(R)-{4-[1-(2-methoxyethyl)piperidin-4-yl]phenyl}(phenyl)methyl]oxy}-4-methylpentanamide;

10 (2S)-N-(cyanomethyl)-4-methyl-2-{[(R)-[4-(6-methyl-1-oxidopyridin-3-yl)phenyl](phenyl)methyl]oxy}pentanamide;

15 (2S)-N-(cyanomethyl)-4-methyl-2-{[(R)-[4-(1-oxidopyridin-4-yl)phenyl](phenyl)methyl]oxy}pentanamide;

(2S)-N-(cyanomethyl)-4-methyl-2-{[(R)-[4-(1-methyl-1-oxidopiperidin-4-yl)phenyl](phenyl)methyl]oxy}pentanamide;

20 (2S)-N-(cyanomethyl)-2-{[(R)-{4-[1-(2-methoxyethyl)-1-oxidopiperidin-4-yl]phenyl}(phenyl)methyl]oxy-4-methylpentanamide;

(2S)-N-(cyanomethyl)-4-methyl-2-{[(R)-[4-(5-methylcyclohex-1-en-1-yl)phenyl](phenyl)methyl]oxy}pentanamide;

25 3-{4-[(R)-[((1S)-1-[(cyanomethyl)amino]carbonyl)-3-methylbutyl]oxy](phenyl)methyl]phenyl}-1-methylpyridinium iodide;

30 (2S)-N-(cyanomethyl)-4-methyl-2-{[(R)-[4-(1-methylpiperidin-3-yl)phenyl](phenyl)methyl]oxy}pentanamide;

(2S)-N-(cyanomethyl)-4-methyl-2-{[(R)-phenyl(4-pyridin-3-ylphenyl)methyl]oxy}pentanamide;

35 (2S)-N-(cyanomethyl)-4-methyl-2-{[(R)-[4-(1-oxidopyridin-3-yl)phenyl](phenyl)methyl]oxy}pentanamide;

(2S)-N-(cyanomethyl)-2-{[(R)-{4-[1-(2-methoxyethyl)piperidin-3-yl]phenyl}(phenyl)methyl]oxy}-4-methylpentanamide;

5 (2S)-N-(cyanomethyl)-4-methyl-2-{[(R)-phenyl(4-quinolin-3-ylphenyl)methyl]oxy}pentanamide;

(2S)-N-(cyanomethyl)-4-methyl-2-{[(R)-[4-(1-methyl-1,2,3,4-tetrahydroquinolin-3-yl)phenyl](phenyl)methyl]oxy} pentanamide;

10 (2S)-N-(cyanomethyl)-4-methyl-2-{[(R)-[4-(1-oxidoquinolin-3-yl)phenyl](phenyl)methyl]oxy}pentanamide;

(2S)-N-(cyanomethyl)-2-{[(R)-{4-[1-(2-methoxyethyl)-1-oxidopiperidin-3-yl]phenyl}(phenyl)methyl]oxy}-4-methylpentanamide;

15 (2S)-N-(1-cyanocyclopropyl)-2-[(R)-[4'-(1-hydroxycyclopropyl)biphenyl-4-yl](phenyl)methoxy]-4-methylpentanamide;

(2S)-N-(1-cyanocyclopropyl)-4-methyl-2-{(R)-phenyl[4'-(2,2,2-trifluoro-1-20 hydroxyethyl)biphenyl-4-yl]methoxy}pentanamide;

(2S)-2-[(R)-[4'-(1-amino-2,2,2-trifluoroethyl)biphenyl-4-yl](phenyl)methoxy]-N-(1-cyanocyclopropyl)-4-methylpentanamide;

25 1-{4'-[(R)-[((1S)-1-{[(1-cyanocyclopropyl)amino]carbonyl}-3-methylbutyl)oxy](phenyl)methyl]biphenyl-4-yl}cyclopropanecarboxylic acid;

2-{4'-[(R)-[((1S)-1-{[(1-cyanocyclopropyl)amino]carbonyl}-3-methylbutyl)oxy](phenyl)methyl]biphenyl-4-yl}-2-hydroxypropanoic acid;

30 (2S)-N-(1-cyanocyclopropyl)-2-[(R)-[4'-(2-hydroxyethyl)biphenyl-4-yl](phenyl)methoxy]-4-methylpentanamide;

(2S)-N-(1-cyanocyclopropyl)-2-[(R)-{4'-[cyclopropyl(hydroxy)methyl]biphenyl-4-35 yl}(phenyl)methoxy]-4-methylpentanamide;

(2S)-N-(1-cyanocyclopropyl)-2-[(R)-[3'-(1-hydroxyethyl)biphenyl-4-yl](phenyl)methoxy]-4-methylpentanamide;

5 (2S)-N-(1-cyanocyclopropyl)-2-[(R)-[3'-(1-hydroxy-1-methylethyl)biphenyl-4-yl](phenyl)methoxy]-4-methylpentanamide;

(2S)-N-(1-cyanocyclopropyl)-2-[(R)-[3'-(1-cyanocyclopropyl)biphenyl-4-yl](phenyl)methoxy]-4-methylpentanamide;

10 (2S)-N-(1-cyanocyclopropyl)-2-[(R)-[4'-(1-cyanocyclopropyl)biphenyl-4-yl](phenyl)methoxy]-4-methylpentanamide;

(2S)-2-[(R)-[3',4'-bis(1-hydroxy-1-methylethyl)biphenyl-4-yl](phenyl)methoxy]-N-(1-cyanocyclopropyl)-4-methylpentanamide;

15 (2S)-2-[(R)-[3',4'-bis(1-hydroxycyclopropyl)biphenyl-4-yl](phenyl)methoxy]-N-(1-cyanocyclopropyl)-4-methylpentanamide;

20 and the pharmaceutically acceptable salts, stereoisomers and N-oxide derivatives thereof.

13. A pharmaceutical composition comprising a compound according to any one of Claims 1 to 12, or a pharmaceutically acceptable salt, stereoisomer or N-oxide derivative thereof, and a pharmaceutically acceptable carrier.

25 14. A pharmaceutical composition made by combining a compound according to any one of Claims 1 to 12, or a pharmaceutically acceptable salt, stereoisomer or N-oxide derivative thereof, and a pharmaceutically acceptable carrier.

30 15. A process for making a pharmaceutical composition comprising combining a compound according to any one of Claims 1 to 12, or a pharmaceutically acceptable salt, stereoisomer or N-oxide derivative thereof, and a pharmaceutically acceptable carrier.

16. A method of inhibiting cathepsin activity in a mammal in need thereof, comprising administering to the mammal a therapeutically effective amount of a compound according to Claim 1.

17. The method according to Claim 16 wherein the cathepsin activity is Cathepsin K activity.

18. A method of treating or preventing a disease selected from: osteoporosis,
5 glucocorticoid induced osteoporosis, Paget's disease, abnormally increased bone turnover, periodontal disease, tooth loss, bone fractures, rheumatoid arthritis, osteoarthritis, periprosthetic osteolysis, osteogenesis imperfecta, metastatic bone disease, hypercalcemia of malignancy or multiple myeloma in a mammal in need thereof by administering to the mammal a therapeutically effective amount of a compound according to Claim 1.

10 19. The method of treating or preventing bone loss in a mammal in need thereof by administering to the mammal a therapeutically effective amount of a compound according to Claim 1.

15 20. A method of treating or preventing osteoporosis in a mammal in need thereof by administering to the mammal a therapeutically effective amount of a compound according to Claim 1.

20 21. A method of treating cathepsin dependent conditions in a mammal in need thereof by administering to the mammal a therapeutically effective amount of a compound according to Claim 1.

25 22. A pharmaceutical composition comprising a compound of any one of Claims 1 to 12, or a pharmaceutically acceptable salt, stereoisomer or N-oxide derivative thereof, and another agent selected from: an organic bisphosphonate, an estrogen receptor modulator, an androgen receptor modulator, an inhibitor of osteoclast proton ATPase, an inhibitor of HMG-CoA reductase, an integrin receptor antagonist, or an osteoblast anabolic agent, and the pharmaceutically acceptable salts and mixtures thereof.

23. A method of treating osteoporosis comprising a compound of Claim 1 and another agent selected from: an organic bisphosphonate, an estrogen receptor modulator, an androgen receptor modulator, an inhibitor of osteoclast proton ATPase, an inhibitor of HMG-CoA reductase, an integrin receptor antagonist, or an osteoblast anabolic agent, and the pharmaceutically acceptable salts and mixtures thereof.

24. A method of treating bone loss comprising a compound of Claim 1 and another agent selected from: an organic bisphosphonate, an estrogen receptor modulator, an androgen receptor modulator, an inhibitor of osteoclast proton ATPase, an inhibitor of HMG-CoA reductase, an integrin receptor antagonist, or an osteoblast anabolic agent, and the pharmaceutically acceptable salts and mixtures thereof.

25. A pharmaceutical composition comprising a compound of any one of Claims 1 to 12, or a pharmaceutically acceptable salt, stereoisomer or N-oxide derivative thereof, and another agent selected from: an organic bisphosphonate, an estrogen receptor modulator, an androgen receptor modulator, an inhibitor of osteoclast proton ATPase, an inhibitor of HMG-CoA reductase, an integrin receptor antagonist, or an osteoblast anabolic agent, and the pharmaceutically acceptable salts and mixtures thereof.

26. A compound of any one of Claims 1 to 12, or a pharmaceutically acceptable salt, stereoisomer or N-oxide derivative thereof, for use in inhibiting cathepsin activity.

27. A compound of any one of Claims 1 to 12, or a pharmaceutically acceptable salt, stereoisomer or N-oxide derivative thereof, for use in treating or preventing osteoporosis.

28. Use of a compound any one of Claims 1 to 12, or a pharmaceutically acceptable salt, stereoisomer or N-oxide derivative thereof, in the manufacture of a medicament for inhibiting cathepsin activity.

29. Use of a compound of any one of Claims 1 to 12, or a pharmaceutically acceptable salt, stereoisomer or N-oxide derivative thereof, in the manufacture of a medicament for treating or preventing osteoporosis.